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ELECTRODES FOR FUNCTIONAL NEUROMUSCULAR STIMULATION

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Section A: Clinical Collaboration

During this quarter, a meeting was held with both primary collaborators, Dr. Peckham (upper extremity) and Dr. Marsolais (lower extremity) to discuss the progress to date with our multiple contact cuff electrodes and to discuss their clinical needs for future motor prostheses. At that meeting, an additional opportunity was presented to discuss electrodes with a wider audience of neural prosthetic researchers at an upcoming conference. An ad hoc session at that conference was organized and held.

Primary Collaborators

The needs of the upper extremity research group center on the selective activation of the muscles that control the hand. With their current system, the biggest problem is intrinsic muscle activation. Epimysial electrodes are placed on muscles in the arm, and while both lateral and palmar grasping patterns are achievable during stimulation, the curl of the fingers due to the intrinsic muscles limits functional grasping ability. Current research in Dr. Peckham's lab is focusing on identifying the muscles that will be needed for better control of the hand. Through that effort, they are designing and fabricating equipment to provide quantitative measurement of hand muscle activation. A short-term (<90 days) implant of a spiral cuff electrode on the ulnar nerve of a patient was discussed. Attempts would be made to selectively stimulate the ulnar nerve to achieve finger extension without thumb abduction.

The needs of the lower extremity group also focus on increased selectivity in muscle activation. Specifically, when a Huntington cuff electrode is placed on the L3 root, both psoas and quadriceps muscle activation is generated, although only psoas activation is desired. Dr. Marsolais would like to move closer to the spinal nerve roots, where there is approximately 1 inch of extradural nerve exposed. Additionally, he would like to place electrodes in the region of the nerve plexus (femoral, lumbar and sacral).

Failure of implanted electrodes within the first few weeks of implant was also a concern. For intramuscular electrodes, the failures stem primarily from the movement of the electrode from its original implant site. Work performed in this laboratory under a previous NIH contract (NO1-NS-0-2395) indicated that stringent cleaning of not only the electrodes, but the implant equipment as well is required for optimal tissue response, healing, and subsequent stabilization of the electrode. The possibility that inadequate cleaning of their implant equipment led to early movement of the electrodes was discussed. For nerve cuff electrodes, failures have been noted in animal studies due to the cuffs actually coming off of the nerve (approximately 25% in a study of 15 cuffs placed in 4 dogs). The reasons the cuffs came off of the nerve are unclear.

The need to move to endoscopic implant of any electrode design was stressed by Dr. Marsolais. Researchers in his lab are designing and fabricating a whole variety of endoscopic implant tools, some of which may be suitable for implant of

either the spiral cuff or the helical spiral cuff electrode.

Both collaborators expressed the desire to have an electrode for afferent recordings. Preliminary laboratory studies have been undertaken to test the ability of a spiral cuff electrode to record afferent information.

Ad Hoc Session

An ad hoc session to discuss problems with electrodes was planned for the Neural Prostheses: Motor Systems IV conference held at Deer Creek Resort, July 23 - 28. Attendees to the conference included researchers, surgeons, and therapists from around the world involved in all areas of neural prosthetics. Participants were invited to attend the session to air their problems with currently available electrodes.

The problems that were raised in the session can be grouped into four categories: Design of Electrodes, Host Response to Neural Prosthetics, Selectivity and Stimulation Methods, and Evaluation and Identification of Neural Prosthetics.

Design of Electrodes

Many people expressed concern over electrode leads. Specifically, whether wound leads or leads coated in silicone tubing were better suited for specific applications, and how to make the choice between the two. Also, how electrode leads can be designed to accommodate growth, more so than cochlear implant electrodes which extend approximately 2 cm, and if there is a better way than to loop extra lead in an implanted silicone bag. How to design leads that provide flexibility in many directions, possibly with straight (unwound) sections for crossing joints or bony prominences, with elastic core materials, and with suture or tube that causes displacement. Finally, is there a way to wind a lead cable with 12 individual wires.

Other discussion on electrodes included the problem of removing electrodes without damaging tissue, the possible alternatives to ethylene oxide sterilization, and the need to develop methods of reducing the risk of infection through antibiotic coating and through management systems. The idea of eliminating long leads and using telemetry to record and transmit was raised, as was the problem of changing recruitment due to external forces applied in areas of implanted electrodes. Finally, the need for standard connectors and leads to make modular component systems was mentioned.

Host Response to Neural Prosthetics

The tissue response to implanted prosthetics was also discussed as a major concern. The selection of electrode materials, material surface area, and stimulus parameters including the possibility of a tolerable DC level was raised. Post-implant hematomas, movement, encapsulation with respect to electric fields, and changing recruitment was also discussed, as was the need to correlate tissue damage with anatomical and physiological function, and determining which of these may be more important. Scarring and the formation of a non-reactive pouch around subcutaneous connectors during lead revision was noted. Also, the anatomical variation among patients, particularly in nerve root location was discussed.

Revision and removal of electrodes was also a worry. Incomplete removal of electrodes and the possibility of inflammatory granuloma formation was discussed. Additionally, the problem of not being able to place a new electrode in the same site as an electrode that had been removed was noted. The question of the need to immobilize limbs after implantation, and whether it is necessary after repositioning of electrodes was raised.

Questions concerning changes in blood supply to tissue and nerves being stimulated were also discussed. Specifically, what kinds of changes occur in muscle or nerve in vicinity of electrodes and the need to investigate and report these.

Selectivity and Stimulation Methods

In terms of selectivity, researchers were concerned with placement of both intramuscular and epimysial electrodes in order to excite more (all) muscle fibers, both in the lower extremity and in the upper extremity. There was also concern over how to minimize pain (spillover) for sensate patients.

Another topic raised was the idea of activating the lumbar sacral portion of the spinal cord to activate a pool of muscles using an electrode array that penetrates the spine. This method would require activation of a complete group without spillover, without damaging the spinal cord, and without movement of the electrode from its proper location. With the idea of stimulating muscle groups, the possibility was raised of using a steering current at low impedance windows in the spinal cord. Finally, it was questioned whether it is individual muscles or movements that are desired.

Evaluation and Identification of Neural Prosthetics

Researchers expressed the desire for tools for in vivo evaluation of both electrodes and nerves. After implantation, researchers would like the ability to measure electrode impedance, as well as to identify individual electrodes and the location of any problems along that electrode. In terms of nerve evaluation, despite chronic animal experiments indicating safety, clinical experience has shown nerves to be damaged and a tool to determine long-term function of the nerve, possibly through nerve latency during stimulation is needed.

In Europe, all implants, leads, stimulators, etc. have identification markings. This should be done in the United States as well, but questions exist about how to do this. Finally, the idea of a database of electrodes, stimulators, researchers, etc. was discussed.

Future Work

A primary collaborator meeting has been planned for the coming quarter. This meeting will focus on the upper extremity research group, and additional researchers from that group will be invited to attend.

Section B: Electrode Design and Fabrication

B.2 Electrode Testing: Testing for Insulation Integrity

Abstract

Careful examination of electrode lead wires from both in vitro and clinical studies has shown pitting corrosion of wire underlying apparently intact insulation (this was reported under a previous NIH Contract, #NO1-NS-0-2395, Final Report). It was suspected that minute insulation flaws were responsible for the corrosion. A simple model was designed and tested for determination of small insulation flaws. The design and testing of this model are presented here.

Summary of Previous Studies

An in vitro experiment was conducted with the intent of establishing that the stimulating tip of an intramuscular electrode was not susceptible to corrosion at maximum pulsing parameters. Ten Peterson-type intramuscular electrodes, fabricated from 21-strand 316L SS wire with Teflon insulation, were continuously pulsed at a frequency of 50Hz, pulsewidth of 200μs, and current amplitude of 25 mA while immersed in a saline solution. After 1000 hours of stimulation, the exposed metal stimulating tips showed no evidence of corrosion. However, isolated spots of discoloration were noted on wire underlying the insulation on several leads. Further examination of these spots revealed pitting corrosion on the wire strands, which likely resulted in the formation of iron oxide.

Three intramuscular electrodes (2 CWRU-type and 1 Peterson, all 7-strand 316L SS wire with Teflon insulation) were removed from a patient completing treatment in our scoliosis study. These electrodes were examined under a dissecting microscope, and similar spots of discoloration were noted along the leads. These spots were further studied using an SEM, and pitting corrosion was found on these wires as well.

Development of Testing Model

The pitting corrosion on these electrodes had not led to their failure. However, if left to propagate, corrosion can lead to electrode failure, formation of unwanted corrosion byproducts, adverse tissue response, and fracture of the lead. Previous work has studied the corrosion-resistance of electrode tips to various stimulation paradigms, and electrode configurations and stimulation parameters have been established to reduce chances of corrosion. However, exposure of the wire leads at sites of small insulation breaches can lead to electrolyte contact, and due to the small surface area, accelerated corrosion can ensue.

While great care is taken in the manufacture of electrodes, insulation flaws either pre-existing or created during manufacture are likely to go undetected. A model has been developed to detect any insulation flaws and reduce the possibility of corrosion along the lead.

The model was developed around two simple hypotheses. The first of these relies on the basic idea of current conduction. If an insulation defect allows metal-

electrolyte contact, current can be passed. This leakage current should be detectable in a simple set-up using a relatively low sensitivity ammeter.

The second hypothesis involves electrochemistry. In standard corrosion cells, the reaction at the site of the cathode involves hydrogen evolution. During corrosion testing of the electrode, and during actual use, there is no DC current driving the circuit, and pulse widths are small enough that hydrogen does not evolve. But by using a constant-voltage source with DC current, hydrogen should evolve at the cathodic site. If the insulated electrode wire has an insulation flaw, and metal-electrolyte contact occurs, hydrogen should evolve at the site of electrolyte contact when the electrode wire is driven cathodically.

Testing and Results of Model

This model was tested in a simple set-up. Six pieces of insulated wire (approximately 15 cm in length) were examined initially for pre-existing flaws. None were found. Defects were created at the midpoint of each of five of these wires using a hypodermic needle, a scalpel blade, and a blunt-tipped instrument, and were of varying size, shape, and severity. The intent of the defects was to damage the overlying insulation, although whether the defects completely penetrated the insulation leaving the wire exposed was unknown. Photographs were taken of each of the flaws following the testing and are presented in Figures B.1- B.5. The sixth wire was left as a control. For comparison, Figures B.6-B.7 are examples of defects in the insulation found in the corroded electrodes reported in the previous progress report (#NO1-NS-0-2395, Final Report).

Phosphate buffered saline was used as the electrolyte solution. The saline was mixed according to the following formula:

4.385 g NaCl 4.021 g Na_2HPO_4 0.5 g NaH_2PO_4 in 500 ml Filtered Water.

Approximately 25 ml of saline solution was placed into each of six flasks.

A schematic of the set-up is provided as Figure B.8. Each of the wires was placed into an individual flask, with the defect area being fully submerged and the two ends of the wire being outside of the flask. A constant voltage, regulated power source was used, with voltage set between 5 and 8 V. The same silver anode wire was used in all tests. The ammeter used had relatively low sensitivity, with the limit of 0.1μA resolution.

DC voltage was maintained in each wire for a few minutes while the set-up was studied for leakage current and bubble formation from hydrogen evolution. In three of the defected wires, immediate bubble formation was noted. A single bubble formed at one site on the wire surface. While this bubble would increase in size, it did not break off on its own. If forced off through sudden motion of the wire, another bubble would immediately form at the same site and again increase in size. For these three wires, current was also detected in the range of 1-100μA. The remaining two defected wires and the control wire showed no evidence of bubble formation or detectable leakage current. These two defected wires were re-tested, again with similar results.

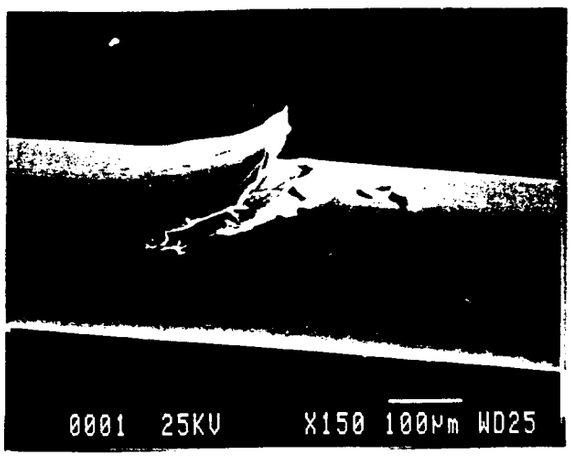

Figure B.1: SEM photo of insulation defect created on Wire #1.

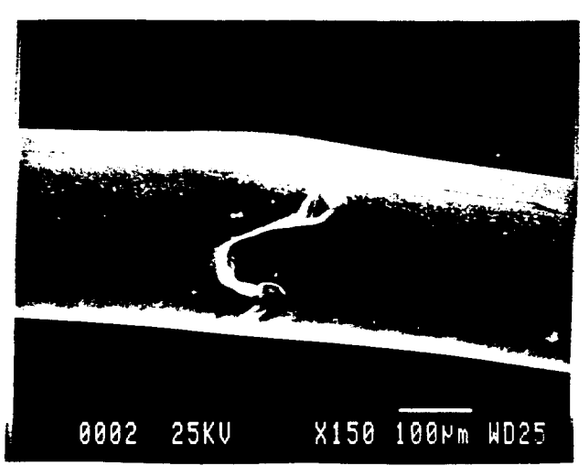

Figure B.2: SEM photo of insulation defect created on Wire #2.

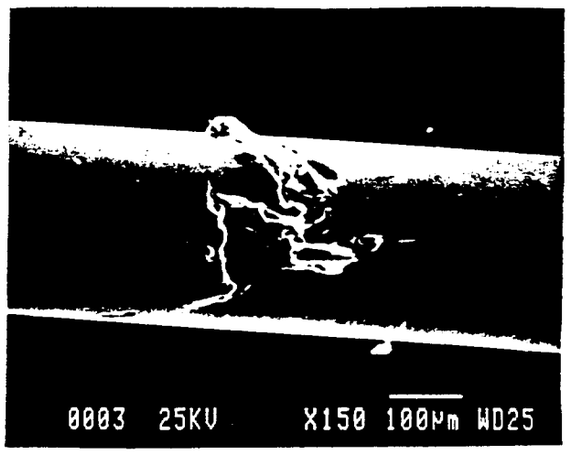

Figure B.3: SEM photo of insulation defect created on Wire #3.

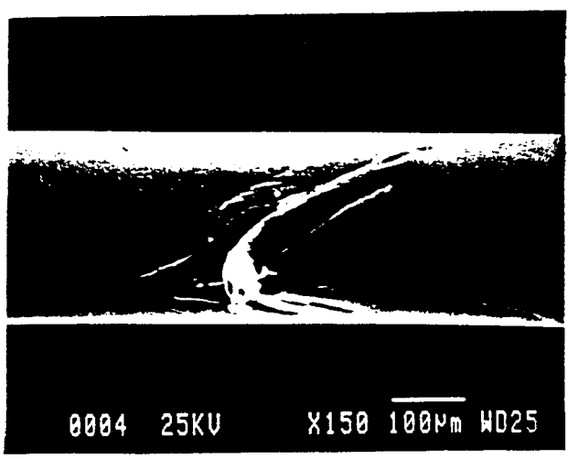

Figure B.4: SEM photo of insulation defect created on Wire #4.

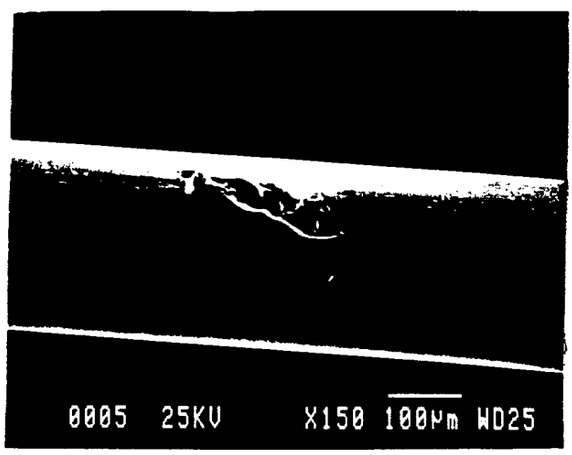

Figure B.5: SEM photo of insulation defect created on Wire #5.

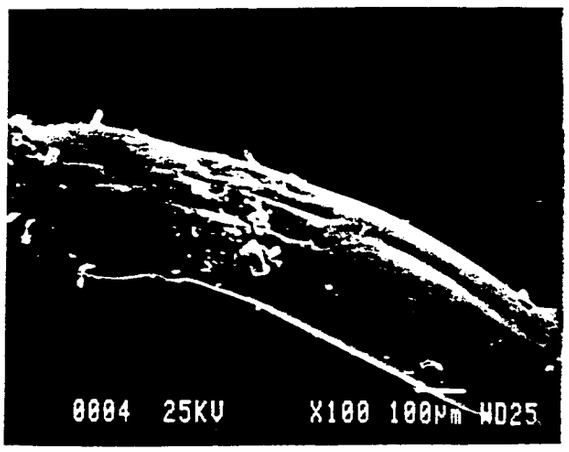

Figure B.6: SEM photo of insulation defect found over corroded wire.

Figure B.7: SEM photo of insulation defect found over corroded wire.

EXPERIMENTAL SET-UP

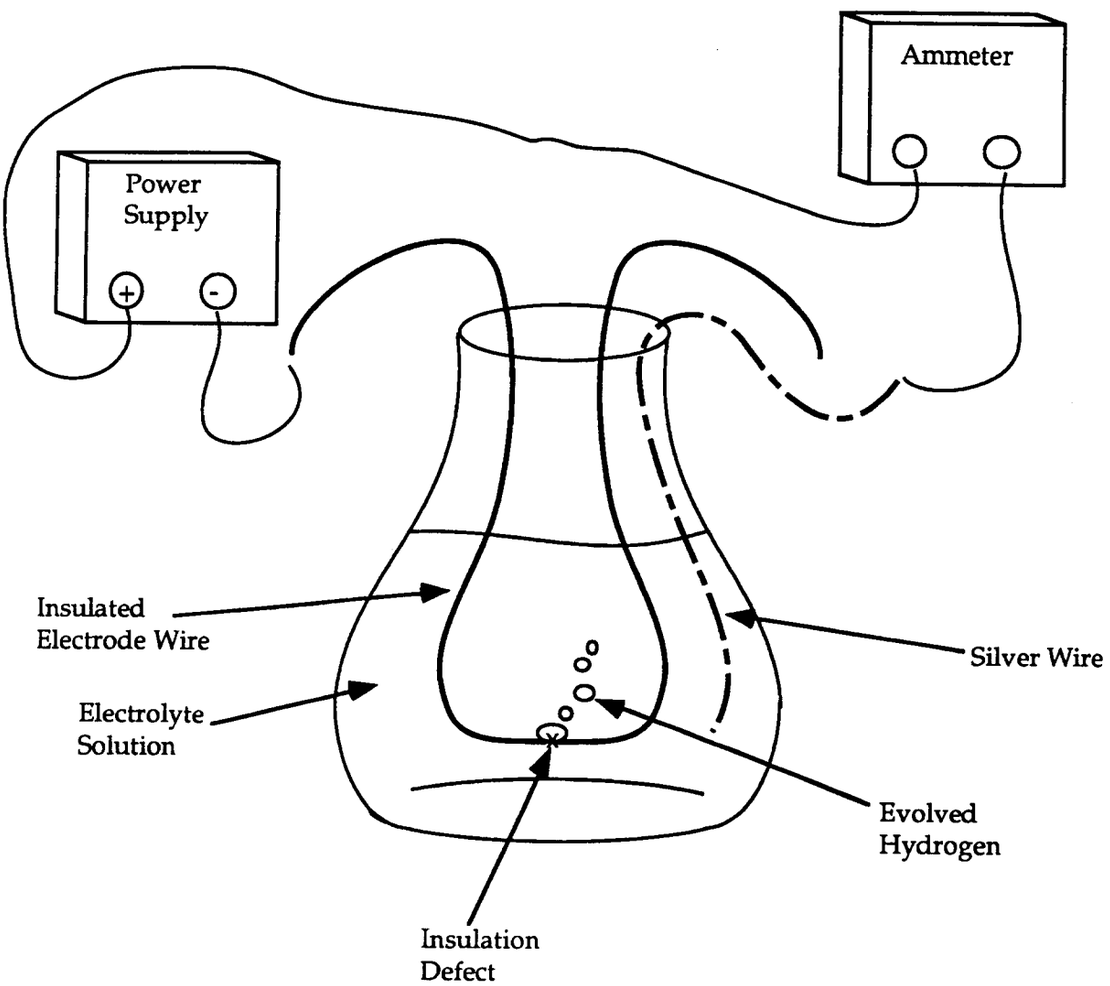

Figure B.8: Schematic of experimental set-up for testing of insulation integrity.

An alternative electrolyte solution was then tested, with hopes of improving surface wettability and increasing metal-electrolyte contact at the defect site. A surfactant was included in the saline solution, following the original recipe, but with the addition of 10 ml of Liquinox. This solution was sonicated for 5 minutes, and then 25 ml amounts were placed in each of six flasks. The same set-up and the original defected wires were again tested. DC voltage was again set at 5V. In this case, four of the defected wires had immediate and rapid bubble formation. The bubbles in this instance were much smaller, were able to break free of the wire and

rise to the surface, but again were immediately replaced by new bubbles. Leakage currents for these four wires were detected in the range of 1-100μA. For the fifth, and notably the smallest defect, no bubbles could be seen. Leakage current for this wire was measured at 1.2μA. The control wire had no evidence of bubble formation or detectable leakage current (<0.1 μA).

The accompanying table summarizes the results of both series of tests on each of the wire strands.

Table B.1:
Summary of Wire Tests

Wire #	Defect Source	Saline current / bubble		Surfactant current / bubble	
#1	scalpel blade	50-100μA	yes	+100μA	yes
#2	hypodermic	no	yes	<100μA	yes
#3	blunt probe	0-30μA	yes	0-100μA	yes
#4	scalpel blade	60-100μA	yes	40μA	yes
#5	blunt probe	no	no	1.2μA	no
#6	control	no	no	no	no

The wire defects were further examined under an SEM and photographed for clearer identification of the defect size. (see previous figures)

The Teflon insulation of this wire, like other insulators, does allow some current leakage. However, this leakage would appear to be less than what is detectable in this simple model (<0.1 μA). Therefore, any detectable leakage current using this set-up is likely due to exposed metal at the site of an insulation breach. Higher resolution ammeters, in the range of nA, pA, and even fA, are available that could provide more detail of the leakage currents, including quantification of the leakage current through intact insulation.

Conclusions

It has long been recognized that the Teflon insulation of the lead wire is not very strong and minimizing electrode handling has been stressed to protect insulation integrity. However, attempts should be made to determine if an

insulation breach is present. This is certainly important in the clinical setting, but should also apply to laboratory testing of the electrodes as well. The simple test procedure described here should protect against unseen insulation flaws that could lead to corrosion and eventual failure of insulated wire leads. From the results of the testing, the saline solution with surfactant should be used to improve surface wettability and identification of small defects. Also, care must be taken to ensure that the stimulating surfaces are not submerged.

B.2 Electrode Testing: Corrosion Testing of Cuff Electrodes

Abstract

In vitro testing of spiral cuff electrodes for corrosion resistance has begun. Three 12-contact spiral cuffs were placed in individual flasks containing approximately 25 ml of phosphate buffered saline solution. One tripole on each cuff is not being stimulated, and will serve as the control. Two tripoles on each cuff are being pulsed at 2 mA, while the other tripole is being used for steering of the opposite tripole, and is being pulsed at 1 mA. Refreshed pure air is pumped over the sealed flasks weekly. Additionally, weekly impedance measurements are being made for all contacts.

Experimental Set-Up

Three spiral cuff electrodes were fabricated according to standard protocol. Minor flaws in each of these cuffs prevented their use in chronic animal experiments, and so they were designated for these in vitro studies.

Prior to the start of the experiment, the electrical continuity between each of the contacts and the leads was confirmed for all cuffs. Additionally, photographs were taken of the opened cuffs. The leads of the cuffs were also tested for insulation integrity, following the method described in the previous section of this progress report. Leads that had evidence of bubble formation or current leakage were designated for controls, or for use in steering. Finally, the cuffs were cleaned following the standard regimen and stored in individual glass petri dishes until the start of the experiment.

A phosphate buffered saline solution was prepared using the following recipe:

2.1925g NaCl (Fisher BP358)
2.0105g Na_2HPO_4 (Fisher S373)
0.25g NaH_2PO_4 (Fisher S369)
in 250ml UltraPure Water (double filtered, double distilled).

Approximately 25 ml of the electrolyte solution was placed in each of three, small Erlenmeyer flasks.

To maintain purity of the set-ups and to avoid contamination, rubber stoppers were placed in the tops of the flasks. In order to have access to the leads of the cuffs, four hypodermic needles were run through the body of each of the stoppers and the leads for the tripoles were fed through these needles (1 tripole per needle). The needles were then removed, leaving the ends of all twelve leads external to the flask. Then, two glass rods were placed into pre-fabricated holes in the stoppers. The glass rods are connected to a tank of pure air, and are used to pump refreshed air into the flasks, replacing any consumed oxygen. The air is pumped in for several minutes once a week.

Three stimulator boards are used to pulse the electrodes. Each of the boards has 4 output stages, with one common ground. These boards are connected to three isolated, independent external power supplies. The boards are programmed to

provide a rectangular pulse, with 50μs pulsewidth, at a frequency of 20Hz, and with a recharge limit of approximately 300μA. The amplitude is set at 2mA for 2 of the tripoles on each cuff, and at 1mA for the steering tripole. The steering is synchronized with its opposite tripole, so that the contact being steered is seeing a total of 3 mA. Table B.2 provides a summary of the stimulation of the tripoles of each cuff. In steering, the center contact is pulsed anodically, and the other two contacts of that tripole are not pulsed. In the tripolar configuration, the center contact is pulsed cathodically, and the other two contacts are pulsed anodically. This occurs for tripoles that are being steered as well.

Table B.2: Summary of Cuff Electrode Stimulation

Electrode		Stimulation	
		Amplitude	Center Contact
Cuff A	Tripole #1	2mA	cathode (steered)
	Tripole #2	-----	control
	Tripole #3	1mA	anode (steering)
	Tripole #4	2mA	cathode
Cuff B	Tripole #1	2mA	cathode (steered)
	Tripole #2	-----	control
	Tripole #3	1mA	anode (steering)
	Tripole #4	2mA	cathode
Cuff C	Tripole #1	2mA	cathode (steered)
	Tripole #2	2mA	cathode
	Tripole #3	1mA	anode (steering)
	Tripole #4	-----	control

An initial check of the electrodes at the time of start-up showed open circuits for all of the contacts. The boards, the pins to the leads, and the electrical continuity between contacts and leads were again checked, and no problems were noted. Finally, it was realized that the wraps of the cuffs were tight enough that the contacts of the cuffs were being covered by the silicone of the previous wrap. A piece of cord, approximately 3 mm in diameter and 5 cm in length was placed within each cuff to serve as a spacer. The cord was purchased at the fabric store, and was placed in alcohol before being wrapped by the cuff. The electrodes were again checked and all contacts are functioning. A schematic of the experimental set-up is provided in

FigureB.9.

The stimulation of the 3 spiral cuff electrodes has recently been started. The contacts for each cuff will be checked for impedance at weekly intervals. If large changes in impedance are noted, the cuff will be examined for any evidence of corrosion. If no large changes in impedance are noted, the cuffs will continue to be pulsed for 3 months. At that time, all remaining cuffs will be examined for evidence of corrosion.

Experimental Set-Up

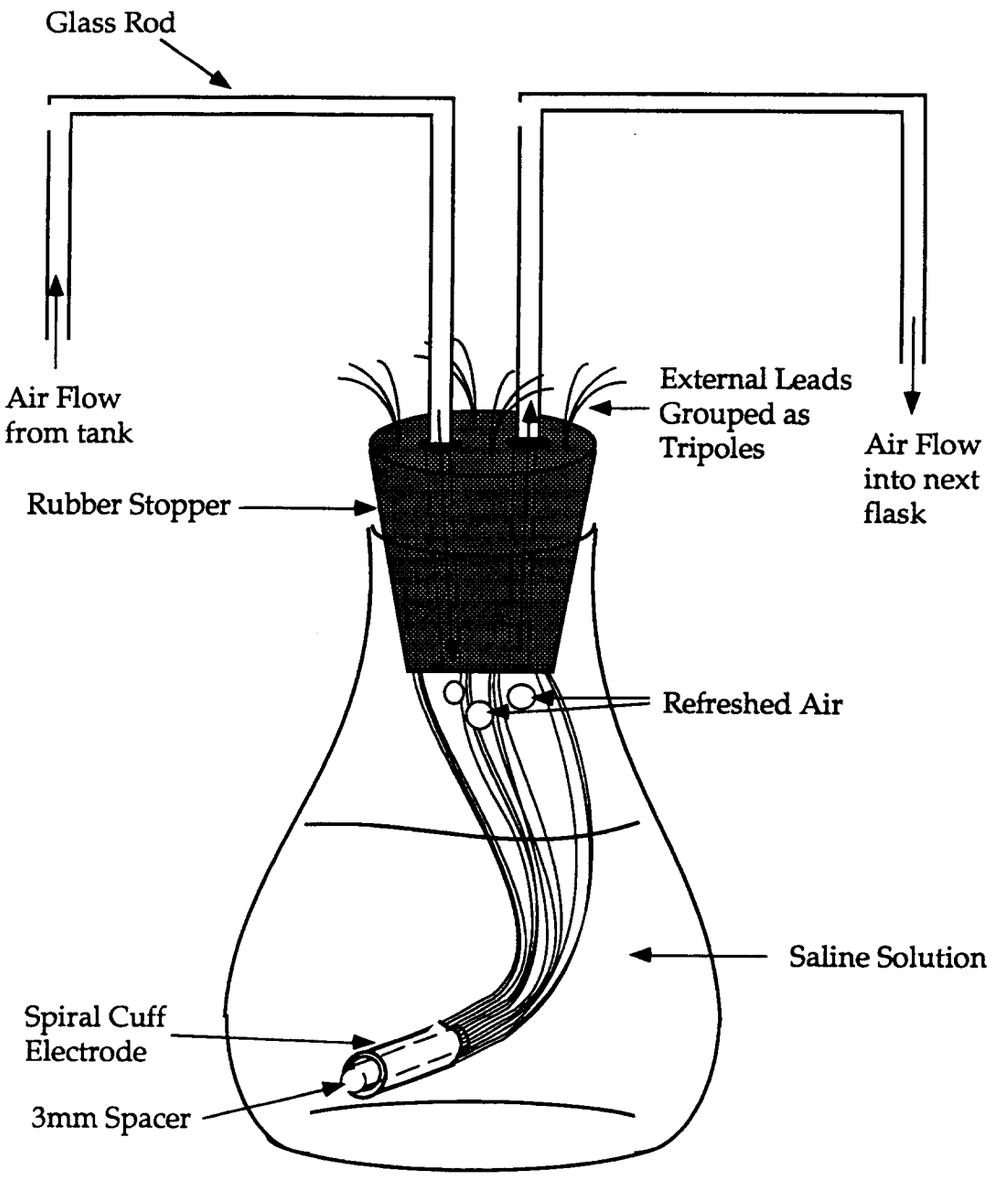

Figure B.9: Schematic of experimental set-up for corrosion testing of spiral cuff electrodes.

Section C: Quantitative Analysis of Electrode Performance in Acute and Chronic Animals

Spiral Cuff Electrodes

In the last two progress reports, details of both the methods and results of the acute animal experiments were provided as manuscripts. The animal work with the spiral cuff electrodes has moved into the chronic stage. Currently, 12 contact spiral cuff electrodes are implanted on the right sciatic nerve of 7 cats. Two of the cats destroyed their lead cables, and are being kept for histological analysis only. The cuffs of the remaining four cats are still functional. Ankle torque for these electrodes are being measured weekly for the first six weeks of implant, and then at 4 week intervals. After a maintenance period of at least 6 months, the cats will be perfused to preserve tissue for histological analysis.

Section C: Quantitative Analysis of Electrode Performance in Acute and Chronic Animals

Helical-spiral Nerve Cuff Electrode

The helical-spiral nerve cuff is a new multiple electrode cuff geometry designed for endoscopic implantation. The curling action of the traditional spiral cuff is duplicated by the helical-spiral cuff electrode to maintain intimate contact with the nerve trunk while allowing for post-surgical swelling and connective tissue growth. In contrast to the grid-like pattern of the contacts in the traditional spiral cuff, the helical-spiral nerve cuff has contact points placed along a line. This reduces the width of the cuff from 12 mm to 3 mm wide. Each tripole of the helical-spiral cuff is formed when the cuff wraps around the nerve and adjacent wraps of the cuff embody adjacent contacts of the tripole. Advantages of this design, besides the smaller width, include grouping all the lead wires together with one exit point and an increase in axial flexibility over the traditional spiral cuff. The grouping of the leads should lead to a more stable electrode that should also produce less mechanical tethering on the nerve trunk.

Acute:
Implant

Helical-spiral nerve cuff electrodes containing two sets of tripoles were constructed according to the procedure outlined in progress report #2. Various sizes were made with diameters ranging between 2.4mm and 3.5mm, to fit a wide range of nerves. At the time of implant the nerve size was measured and the cuff corresponding to the nearest size was implanted.

Results

In acute animal testing of the multiple contact **helical-spiral** cuff electrode, we have found that we can control dorsiflexion and plantarflexion with both monopolar and tripolar electrode configurations, as illustrated in Figure C.1. In the left graph, two curves from monopolar stimulation are shown. The curve labeled 'monopole #3' uses contact #3 as a cathode with a distant anode and primarily shows recruitment of plantar flexors. The curve labeled 'monopole #4' uses contact #4 as a cathode with a distant anode and shows recruitment of the dorsi flexors. The right graph has two recruitment curves from tripolar stimulation. The first recruitment curve, labeled 'tripole 1-3', is the tripole configuration using contact #3 as the cathode with the two contacts on wire #1 as the associated anodes. Similarly, the curve labeled 'tripole 2-4' is the tripole configuration using contact #4 as the cathode and the two contacts on the #2 wire as its associated anodes (see Figure C.2). The 1-3 tripole configuration was found to recruit plantarflexors and the 2-4 tripole configuration was found to recruit dorsiflexors. As expected, each tripole appears to recruit more fibers before spill-over. This is shown in the graphs by the recruitment curves reaching a higher magnitude of torque before spill-over.

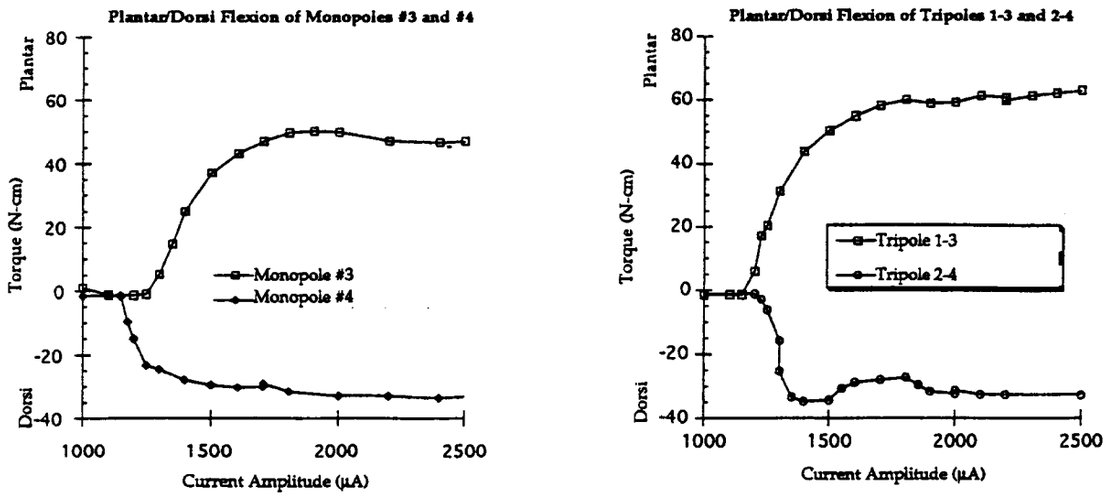

Figure C.1: Graphs of monopolar stimulation on the **left** and the corresponding tripoles on the **right**, i.e. tripole 1-3 uses monopole #3 as its cathode, and tripole 2-4 uses monopole #4 as its cathode.

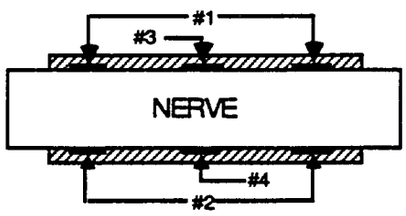

Figure C.2: Diagram of tripolar configurations. Tripole 1-3 uses contact #3 as a cathode and the two contacts from wire #1 as the anodes. Similarly, tripole 2-4 uses contact #4 cathodically and the two contacts from wire #2 anodically.

Chronic

We have implanted a leadless helical-spiral cuff on the left sciatic nerve of each of the six cats used in the chronic study. These cuffs will be explanted at the same time as the spiral cuff electrodes to evaluate the structure and cellular morphology of the encapsulation tissue and to assess the response of the neural tissue to the presence of the electrode. The implantation procedure was found to be straightforward with the exception that the end of the cuff tended to curl onto itself. Future modifications to this cuff electrode could include a thin sheet of polyimid near the tip of the cuff to add stiffness and prevent excessive curling. This extra

stiffness should aid in the implantation and allow the electrode to lay flatter on the nerve trunk.

We are currently working on tools to allow endoscopic placement of the electrode around a nerve. One design uses saline or air jets to inject the cuff electrode out of a cartridge and onto the nerve trunk. As the helical-spiral cuff electrode protrudes from the cartridge, it begins to wrap and push itself around the nerve trunk. A second idea is a tool that actually wraps itself around the nerve trunk with the cuff electrode attached and then the cuff electrode is released already around the nerve.

The chronic animal work was also supported by the Paralyzed Veterans Association department of the Spinal Cord Research Foundation.